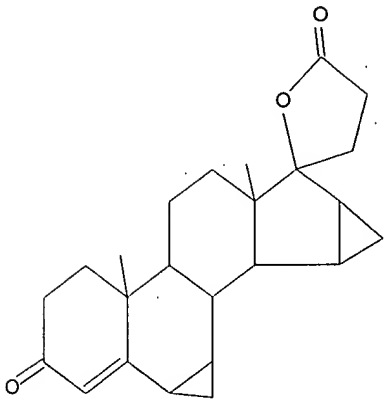
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 exa full

FULL SEARCH INITIATED 15:21:22 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 63 TO ITERATE

100.0% PROCESSED 63 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

L2 5 SEA EXA FUL L1

=> d l2 1-5 abs ibib hitstr

'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'IBIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract

APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS --ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

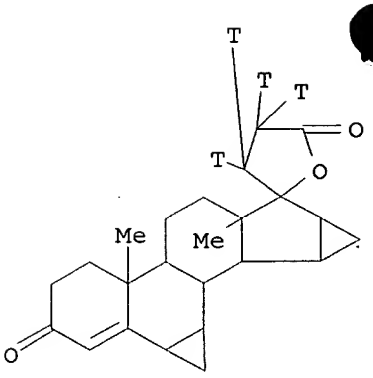
For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):iall

L2 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 102974-48-1 REGISTRY
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione-4',5'-t2,
1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-3',4'-t2-10,13-dimethyl-,
[6R-(6.alpha.,7.alpha.,8.beta.,9.alpha.,10.beta.,13.beta.,14.alpha.,15.alpha.,16.alpha.,17.beta.)]- (9CI) (CA INDEX NAME)
MF C24 H26 O3 T4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C3-C3-C4O-C5-C6-C6-C6	C3-C3-OC4-C5-C6-C6-C6	3-3-5-5-6-6-6	C22O	21803.1.1	1



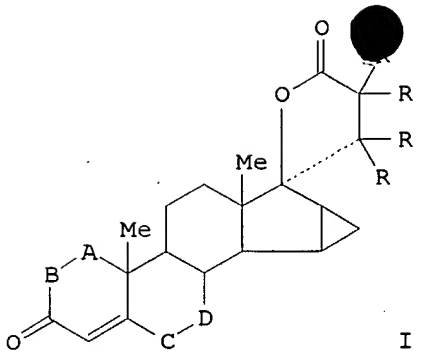
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 105:43156 CA
TITLE: Multiply tritiated steroid-20,17-spirolactones and their use as tracer substances
INVENTOR(S): Schulze, Paul Eberhard; Nickisch, Klaus; Laurent, Henry; Pollow, Kunhard
PATENT ASSIGNEE(S): Schering A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: C07J021-00
SECONDARY: A61K049-00
CLASSIFICATION: 32-5 (Steroids)
Section cross-reference(s): 1
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3414508	A1	19851024	DE 1984-3414508	19840413
EP 158365	A2	19851016	EP 1985-104470	19850412
EP 158365	A3	19860910		
EP 158365	B1	19890913		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AU 8541098	A1	19851017	AU 1985-41098	19850412
AU 589120	B2	19891005		
JP 61005094	A2	19860110	JP 1985-76857	19850412
AT 46312	E	19890915	AT 1985-104470	19850412
US 4904462	A	19900227	US 1985-722255	19850412
PRIORITY APPLN. INFO.:			DE 1984-3414508	19840413
			EP 1985-104470	19850412

GRAPHIC IMAGE:



I  =Q  =Q1

ABSTRACT:
Spirolactones I [AB = CH2CH2, CH:CH, Q; CD = Q1, CH2CHCO2(CH2)nCR3; R = H, T; n
= 0, 1], useful as tracer substances for mineralocorticoids, were prepd. 17.alpha.-(3-Hydroxy-1-propynyl)-6.beta.,7.beta.:15.beta.,16.beta.-dimethylene-
5.beta.-androstane-3.beta.,5,17.beta.-triol was tritiated with 3H2 over Pd/CaCO3 to give 17.alpha.-(3-hydroxypropyl-2,2,3,3-t4)-
6.beta.,7.beta.:15.beta.,16.beta.-dimethylene-5.beta.-androstane-
3.beta.,5,17.beta.-triol, which was treated with pyridinium dichromate to give 6.beta.,7.beta.:15.beta.,16.beta.-dimethylene-3-oxo-17.alpha.-pregn-4-ene-
18,18,19,19-t4 20,17-carbolactone. This was dehydrogenated to the corresponding pregna-1,4-diene (II) with dichlorodicyanobenzoquinone. II had a
relative bonding affinity of 90 for mineralocorticoid receptor, compared to 100
for aldosterone. Bonding affinities of selected I for glucocorticoid and progesterone receptor as well as serum-CBG were tabulated.

SUPPL. TERM: pregnene spirolactone tritiated mineralocorticoid receptor tracer; glucocorticoid receptor tracer tritiated pregnene spirolactone; progesterone receptor tracer tritiated pregnene spirolactone

INDEX TERM: Receptors
ROLE: RCT (Reactant)
(for mineralocorticoids, glucocorticoids, and progesterone, tritiated pregene spirolactones as tracers for)

INDEX TERM: Steroids, preparation
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of tritiated pregnene spirolactone derivs., as receptor tracers)

INDEX TERM: Isotope indicators
(tritiated pregnene spirolactones, for mineralo- and glucocorticosteroid and progesterone receptors)

INDEX TERM: Corticosteroids, biological studies
ROLE: BIOL (Biological study)
(gluco-, tritiated pregnene spirolactones as tracers for receptors of)

INDEX TERM: Corticosteroids, biological studies
ROLE: BIOL (Biological study)
(mineralo-, tritiated pregnene spirolactones as tracers for receptors of)

INDEX TERM: 50630-93-8
ROLE: RCT (Reactant)
(methylation by, of carboxypregnene derivs.)

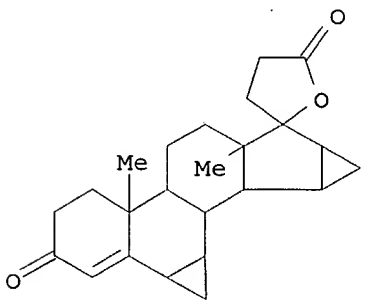
INDEX TERM: 102974-48-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dehydrogenation of)

INDEX TERM: 102[illegible]4-47-0P
ROLE: [illegible] (Reactant); SPN (Synthetic p[illegible]aration); PREP (Preparation)
(prepn. and oxidn. of)
INDEX TERM: 102974-53-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn.-cyclization of)
INDEX TERM: 102974-46-9P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
INDEX TERM: 102974-49-2P 102974-51-6P 102974-54-9P 102974-55-0P
102974-56-1P 102988-43-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as mineralocorticoid receptor tracer)
INDEX TERM: 57-83-0P, preparation
ROLE: PREP (Preparation)
(tritiated pregnene spirolactones as tracers for receptors of)
INDEX TERM: 10028-17-8, reactions
ROLE: RCT (Reactant)
(tritiation by, of (hydroxypropynyl)androstanetriol deriv.)
INDEX TERM: 82543-17-7 102974-52-7
ROLE: RCT (Reactant)
(tritiation of)
INDEX TERM: 84529-98-6 102974-50-5
ROLE: RCT (Reactant)
(tritritiomethylation of)

L2 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 93920-59-3 REGISTRY
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H30 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C3-C3-C4O-C5-C6-C6-C6	C3-C3-OC4-C5-C6-C6-C6	3-3-5-5-6-6-6	C22O	21803.1.1	1



1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 102:24922 CA
TITLE: 3-(3-Oxo-4-unsaturated steroid-17.alpha.-yl)propionic acid lactones
INVENTOR(S): Junghans, Klaus
PATENT ASSIGNEE(S): Schering A.-G. , Fed. Rep. Ger.
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.: C07J021-00
CLASSIFICATION: 32-5 (Steroids)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3306554	A1	19840823	DE 1983-3306554	19830222
EP 117507	A1	19840905	EP 1984-101780	19840221
EP 117507	B1	19871111		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 30728	E	19871115	AT 1984-101780	19840221
JP 59205398	A2	19841120	JP 1984-30491	19840222
JP 03069359	B4	19911031		
US 4507238	A	19850326	US 1984-582644	19840222
PRIORITY APPLN. INFO.:			DE 1983-3306554	19830222
			EP 1984-101780	19840221

GRAPHIC IMAGE: For diagram(s), see printed CA Issue.
ABSTRACT:
Title lactones I (Q = cyclopentaphenanthrene moieties) were prepd. by hydrogenation-oxidn. of propargyl alcs. II. Thus, hydrogenation of androstenylpropargyl alc III in THF contg. Raney Ni and treatment of the reaction product with Jones reagent for 5 min at 0.degree. gave the lactone IV.

SUPPL. TERM: propionic acid lactone steroidal; spirofuranone androstene
INDEX TERM: Steroids, preparation
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, of propionic acid lactones, by hydrogenation-oxidn. of hydroxy propargyl alc. derivs.)
INDEX TERM: 107-19-7
ROLE: RCT (Reactant)
(addn. reaction of, with methyleneandrostenedione)
INDEX TERM: 55542-26-2 82543-17-7
ROLE: RCT (Reactant)
(hydrogenation-oxidn. of, lactone from)
INDEX TERM: 82543-16-6
ROLE: RCT (Reactant)
(oxidn. of)
INDEX TERM: 93771-35-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and addn. reaction of, with propargyl alc.)
INDEX TERM: 93771-34-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenation-oxidn. of)
INDEX TERM: 976-70-5P 93920-59-3P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

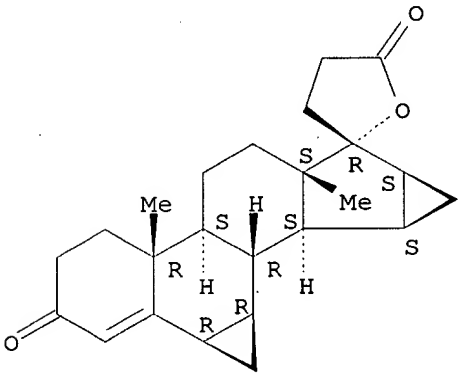
L2 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2000 ACS

RN 90457-65-1 REGISTRY
CN Spiro[17H-dicyclo[b]pa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-, [6R-(6.alpha.,7.alpha.,8.beta.,9.alpha.,10.beta.,13.beta.,14.alpha.,15.alpha.,16.alpha.,17.alpha.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H30 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT
(*File contains numerically searchable property data)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C3-C3-C4O-C5-C6-C6-C6	C3-C3-OC4-C5-C6-C6-C6	3-3-5-5-6-6-6	C22O	21803.1.1	1

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 102:215401 CA
TITLE: Structure-activity relationship of spironolactone derivates. Correlation of the affinity for rat renal mineralocorticoid receptors in vitro and the antialdosterone activity in the adrenalectomized rat in vivo
AUTHOR(S): Wambach, Gerhard; Casals-Stenzel, Jorge
CORPORATE SOURCE: Med. Klin. Koel-Merheim Med. Poliklin., Univ. Koelin, Cologne, Fed. Rep. Ger.
SOURCE: Adrenal Steroid Antagonism, Proc. - Satell. Workshop Int. Congr. Endocrinol. (1984), 291-313. Editor(s): Agarwal, Manjul K. de Gruyter: Berlin, Fed. Rep. Ger.
CODEN: 53KFAF
DOCUMENT TYPE: Conference
LANGUAGE: English
CLASSIFICATION: 2-3 (Mammalian Hormones)

ABSTRACT:
The ability of 17 ste[redacted]ds with structures similar to [redacted]ronolactone [52-01-7]
to compete with 3H-labeled aldosterone [52-39-1] for binding at rat renal cytoplasmic receptors in vitro and the antialdosterone activity in adrenalectomized rats in vivo were compared with that of spironolactone. Replacement of the 17-spirolactone ring by a 17.alpha.-hydroxypropyl group and a 17.beta.-hydroxyl group resulted in a loss of receptor affinity without a redn. in antialdosterone action in vivo. Compared to spironolactone, C6/C7 unsatd. compds. showed a reduced activity both in vitro and in vivo. Substitution of the 7.alpha.-thioacetyl group in the .beta.-position (prorenone
[40574-52-5]) increased the in vivo as well as the in vitro activity by 41 and 52%, resp. Introduction of a Me group in the D-ring resulted in a similar redn. in activity both in vivo and in vitro. Spirorenone [74220-07-8] and 2 of its derivs. were 3-8 times more potent than spironolactone. Their receptor affinity was only slightly increased. Taken together, measuring the receptor affinity does not replace testing the in vivo antimineralocorticoid activity of
new compds. Comparison between affinity for mineralocorticoid receptors and biol. activity however, provides insights into the metab. of potential antimineralocorticoids.

SUPPL. TERM: spironolactone deriv structure activity; mineralocorticoid receptor spironolactone deriv; antialdosterone spironolactone deriv

INDEX TERM: Receptors
ROLE: BIOL (Biological study)
(for mineralocorticosteroids, spironolactone derivs. binding by, structure in relation to)

INDEX TERM: Kidney, composition
(mineralocorticosteroid receptor of, spironolactone derivs. binding by)

INDEX TERM: Corticosteroids, biological studies
ROLE: BIOL (Biological study)
(mineralo-, inhibitors of, spironolactone derivs. as, structure in relation to)

INDEX TERM: Molecular structure-biological activity relationship
(mineralocorticosteroid receptor-binding, of spironolactone analogs)

INDEX TERM: Molecular structure-biological activity relationship
(mineralocorticosteroid-antagonizing, of spironolactone analogs)

INDEX TERM: 52-01-7 976-71-6 40574-52-5 49848-01-3 65049-57-2 65928-43-0 65928-46-3 67372-58-1 67392-87-4 69651-50-9 74220-07-8 81826-19-9 81826-20-2 81826-21-3 81830-36-6 86533-13-3 90376-21-9 90457-65-1
ROLE: BIOL (Biological study)
(antimineralocorticosteroid and mineralocorticosteroid receptor-binding activity of, structure in relation to)

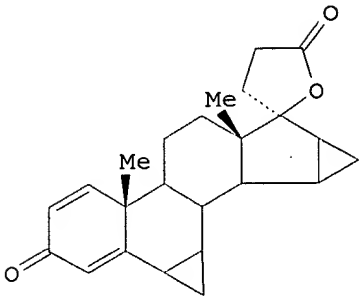
INDEX TERM: 52-39-1
ROLE: BIOL (Biological study)
(receptor binding of, in kidney, spironolactone derivs. effect on)

REFERENCE 2

ACCESSION NUMBER: 101:932 CA
TITLE: The renal action of spirorenone and other 6.beta.,7.beta.; 15.beta.,16.beta.-dimethylene-17-spirolactones, a new type of steroidal aldosterone antagonists
AUTHOR(S): Casals-Stenzel, J.; Buse, M.; Wambach, G.; Losert, W.
CORPORATE SOURCE: Res. Lab., Schering A.-G., Berlin, D-1000/65, Fed.

SOURCE: [redacted] Rep. Ger.
Arzneim.-Forsch. (1984), 34[redacted]241-6
CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 2-2 (Mammalian Hormones)
GRAPHIC IMAGE:



I

ABSTRACT:
Spirorenone (I) [74220-07-8] was 8.6-fold more potent than spironolactone [52-01-7] in its antialdosterone activity in adrenalectomized rats, as measured
by the ability to antagonize the effects of i.v. aldosterone [52-39-1] on urinary mineral excretion. However, I had a lower in vitro affinity for the mineralocorticoid receptors of rat kidney. Three I derivs. exhibited antialdosterone activities between those of I and spironolactone, even though one showed a mineralocorticoid receptor affinity that was double that of spironolactone. A deriv. with a reversed configuration of the 17-spirolactone ring had no biol. activity in either test.

SUPPL. TERM: spirorenone aldosterone antagonist; spirolactone steroidal aldosterone antagonist
INDEX TERM: Receptors
ROLE: BIOL (Biological study)
(for mineralocorticosteroids, spirorenone and spirenone derivs. binding by, aldosterone-antagonizing activity in relation to)
INDEX TERM: Resorption
(of potassium and sodium, aldosterone antagonists effect on)
INDEX TERM: Corticosteroids, biological studies
ROLE: BIOL (Biological study)
(mineralo-, receptors for, spirorenone and spirorenone derivs binding by, aldosterone antagonist activity in relation to)
INDEX TERM: Molecular structure-biological activity relationship
(mineralocorticosteroid-antagonizing, of spirorenones)
INDEX TERM: 67392-87-4 69651-50-9 74220-07-8 90376-21-9 90457-65-1
ROLE: BIOL (Biological study)
(aldosterone-antagonizing activity of, mineralocorticoid receptor affinity in relation to)
INDEX TERM: 52-01-7
ROLE: BIOL (Biological study)
(aldosterone-antagonizing activity of, spirorenone and spirorenone derivs. in relation to)
INDEX TERM: 7440-09-7, biological studies 7440-23-5, biological studies
ROLE: BIOL (Biological study)
(excretion of, aldosterone antagonists effect on)

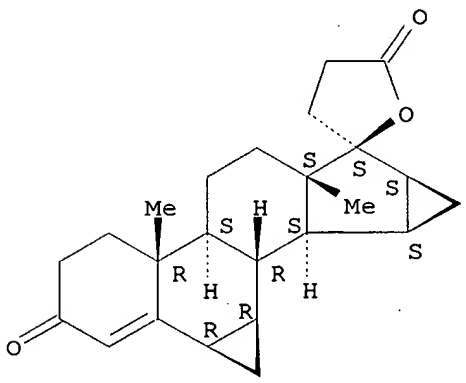
INDEX TERM: [redacted]-1
ROL[redacted]U (Biological study, unclass[redacted]); BIOL (Biological study)
(inhibitors, spirorenone and spirorenone derivs. as)

L2 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 67392-87-4 REGISTRY
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-, (2'S,6R,7R,8R,9S,10R,13S,14S,15S,16S)-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-,
[6R-(6.alpha.,7.alpha.,8.beta.,9.alpha.,10.beta.,13.beta.,14.alpha.,15.alpha.,16.alpha.,17.beta.)]-
OTHER NAMES:
CN 1,2-Dihydrospirorenone
CN 3-Oxo-6.beta.,7.beta.:15.beta.,16.beta.-dimethylene-17.alpha.-pregn-4-en-21,17-carbolactone
CN Dihydrospirorenone
CN Drospirenone
CN ZK 30595
FS STEREOSEARCH
MF C24 H30 O3
CI COM
LC STN Files: ADISINSIGHT, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMLIST, CIN, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C3-C3-C4O-C5- C6-C6-C6	C3-C3-OC4-C5- C6-C6-C6	3-3-5-5-6-6- 6	C22O	21803.1.1	1

Absolute stereochemistry.



59 REFERENCES IN FILE CA (1967 TO DATE)
59 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1 [redacted] [redacted]

ACCESSION NUMBER: 133:276797 CA
TITLE: Low dose estrogen interrupted hormone replacement therapy
INVENTOR(S): Casper, Robert F.; Shangold, Gary A.; Ausmanas, Militza K.
PATENT ASSIGNEE(S): Jencap Research Ltd., Can.; Ortho-McNeil Pharmaceutical Inc.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61P005-24
SECONDARY: A61K031-565
CLASSIFICATION: 2-4 (Mammalian Hormones)
Section cross-reference(s): 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059577	A1	20001012	WO 2000-CA315	20000322

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-126970 19990330
ABSTRACT:
A pharmaceutical prepn. for hormone replacement therapy comprises a plurality of daily doses for alternating a relatively dominant estrogenic activity phase comprising three daily doses of a substance exhibiting estrogenic activity equiv. to about 1 mg/day of 17.beta.-estradiol, and a relatively dominant progestogenic activity phase of a combination of a substance exhibiting estrogenic activity equiv. to about 1 mg/day of 17.beta.-estradiol and a substance exhibiting progestogenic activity equiv. to about 90 .mu.g/day of norgestimate. The active ingredients are compounded with the chosen carrier to
form tablets which are packaged in accordance with the chosen regimen. For example, the low-dose estrogen regimen of the present invention contg. 1 mg estradiol and 90 .mu.g norgestimate resulted in a mean decrease in the no. of hot flashes per day of 94.9% compared to baseline. The ref. or Kliogest regimen contg. 2 mg estradiol reduced hot flashes by a mean 92.8% and the 2 mg interrupted estradiol reduced hot flashes by 92.5%.

SUPPL. TERM: estrogen progestogen interrupted hormone replacement therapy
INDEX TERM: Globulins, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(SHBG (sex hormone-binding globulin), lack of affinity for; low-dose estrogen interrupted hormone replacement therapy with reduced risk of cancer)
INDEX TERM: Progesterone receptors
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(binding to; low-dose estrogen interrupted hormone replacement therapy with reduced risk of cancer)

INDEX TERM: H[redacted]ne replacement therapy
[redacted]ow-dose estrogen interrupted [redacted]one replacement therapy with reduced risk of cancer)
INDEX TERM: Estrogens
ROLE: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-dose estrogen interrupted hormone replacement therapy with reduced risk of cancer)
INDEX TERM: Progestogens
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-dose estrogen interrupted hormone replacement therapy with reduced risk of cancer)
INDEX TERM: Androgen receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(poor affinity for; low-dose estrogen interrupted hormone replacement therapy with reduced risk of cancer)
INDEX TERM: Drug delivery systems
(tablets; oral compns. contg. low-dose estrogen for interrupted hormone replacement therapy with reduced risk of cancer)
INDEX TERM: 50-27-1, Estriol 50-27-1D, Estriol, esters 50-28-2, 17.beta.-Estradiol, biological studies 50-28-2D, Estradiol, esters 53-16-7, Estrone, biological studies 57-63-6D, 17.alpha.-Ethinylestradiol, esters and ethers 68-23-5, Norethynodrel 71-58-9, Medroxyprogesterone acetate 72-33-3, Mestranol 152-43-2, Quinestrol 152-62-5, Dydrogesterone 302-22-7, Chlormadinone acetate 427-51-0, Cyproterone acetate 481-97-0, Estrone sulfate 595-33-5, Megestrol acetate 7280-37-7, Piperazine estrone sulfate 35189-28-7, Norgestimate 54024-22-5, Desogestrel 58691-88-6, Nomegestrol 60257-22-9 65928-58-7, Dienogest 67392-87-4, Drospirenone 74513-62-5, Trimegestone
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low-dose estrogen interrupted hormone replacement therapy with reduced risk of cancer)
REFERENCE COUNT: 10
REFERENCE(S):
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(3) Jenapharm Gmbh; DE 4429374 C 1996
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REFERENCE 2

ACCESSION NUMBER: 133:145031 CA
TITLE: Inhibition of ovulation by a novel progestogen

(drospirenone) alone or in [redacted]bination with ethinylestradiol

AUTHOR(S): Rosenbaum, P.; Schmidt, W.; Helmerhorst, F. M.; Wuttke, W.; Rossmanith, W.; Freundl, F.; Thomas, K.; Grillo, M.; Wolf, A.; Heithecker, R.

CORPORATE SOURCE: Universitatskliniken des Saarlandes, Frauenklinik und Poliklinik, Homburg, 66421, Germany

SOURCE: Eur. J. Contracept. Reprod. Health Care (2000), 5(1), 16-24
CODEN: ECRCFK; ISSN: 1362-5187

PUBLISHER: Parthenon Publishing Group Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 2-3 (Mammalian Hormones)

ABSTRACT:

Studies were carried out to investigate ovulation inhibition with drospirenone, a novel progestogen that has a profile similar to natural progesterone, when given alone or in combination with ethinylestradiol. Hormonal parameters (LH, FSH, 17.beta.-estradiol and progesterone) and peripheral parameters (cervical score, spinnbarkeit and crystn.), as well as follicle size assessed by ultrasonog., were measured in two groups of healthy women. Forty-eight women aged 19-35 yr were randomly assigned to receive 0.5 mg, 1.0 mg, 2.0 mg or 3.0 mg of drospirenone over a single treatment cycle, and 52 women aged 20-35 yr were randomized to receive either 2 mg drospirenone/30 .mu.g ethinylestradiol or 3 mg drospirenone/30 .mu.g ethinylestradiol over three treatment cycles. Baseline measurements were taken during a control pretreatment cycle. Adequate ovarian suppression with drospirenone alone was evident at dose levels of 2 and 3 mg, and at 3 mg all subjects had anovulatory cycles. Although both combined prepns. (2 mg and 3 mg drospirenone/30 .mu.g ethinylestradiol) inhibited the hypothalamic-pituitary-ovarian axis, follicular maturation leading to escape ovulation was obsd. in three subjects in the 2 mg drospirenone/30 .mu.g ethinylestradiol group. Only one of these ovulations was considered to be definitely the result of treatment failure. All cycles in the 3 mg drospirenone/30 .mu.g ethinylestradiol group were anovulatory. No statistically significant difference was found between treatment groups. The combination of 3 mg drospirenone/30 .mu.g ethinylestradiol (Yasmin, Schering AG) reliably inhibits ovulation, with a low frequency of follicular maturation, and provides a reasonable safety margin.

SUPPL. TERM: ovulation inhibition hormone drospirenone ethinylestradiol oral contraceptive

INDEX TERM: Endocrine system
(anterior pituitary-hypothalamus-ovary; ovulation inhibition and hormonal response to drospirenone alone or in combination with ethinylestradiol in women)

INDEX TERM: Uterus
(cervix; ovulation inhibition and hormonal response to drospirenone alone or in combination with ethinylestradiol in women)

INDEX TERM: Ovary
(follicle; ovulation inhibition and hormonal response to drospirenone alone or in combination with ethinylestradiol in women)

INDEX TERM: Contraceptives
(oral; ovulation inhibition and hormonal response to drospirenone alone or in combination with ethinylestradiol in women)

INDEX TERM: Ovulation
(ovulation inhibition and hormonal response to drospirenone alone or in combination with

[redacted]hinylestradiol in women)
INDEX TERM: 67[redacted]-87-4, Drospirenone 164017-1[redacted], Yasmin
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation inhibition and hormonal response to drospirenone alone or in combination with ethinylestradiol in women)
INDEX TERM: 50-28-2, 17.beta.-Estradiol, biological studies 57-83-0, Progesterone, biological studies 9002-67-9, LH 9002-68-0, FSH
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ovulation inhibition and hormonal response to drospirenone alone or in combination with ethinylestradiol in women)
REFERENCE COUNT: 11
(1) Fuhrmann, U; Contraception 1996, V54, P243 CAPLUS
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(3) Krattenmacher, R; Acta Endocrinol 1992, V124, P88
(4) Losert, W; Arzneim Forsch/Drug Res 1985, V35, P459 CAPLUS
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(6) Nickisch, K; J Med Chem 1991, V34, P2464 CAPLUS
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REFERENCE 3

ACCESSION NUMBER: 133:115266 CA
TITLE: An open-label, multicenter study to evaluate Yasmin, a low-dose combination oral contraceptive containing drospirenone, a new progestogen
AUTHOR(S): Parsey, K. S.; Pong, A.
CORPORATE SOURCE: Berlex Laboratories, Montville, NJ, USA
SOURCE: Contraception (2000), 61(2), 105-111
CODEN: CCPTAY; ISSN: 0010-7824
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 2-3 (Mammalian Hormones)
ABSTRACT:
This open-label, multicenter study evaluated the efficacy, safety, and cycle control of Yasmin, a new low-dose, monophasic oral contraceptive contg. the unique progestogen drospirenone (DRSP) 3 mg and ethinyl estradiol (EE) 30 .mu.g. DRSP is a synthetic progestogen that has antiandrogenic and antimineralocorticoid effects. In this study, 326 women were evaluated and 220 (67%) completed all 13 treatment cycles. The cor. Pearl Index was 0.407. Of the 151 subjects who experienced intermenstrual bleeding at any time during the study, the majority (64%) had bleeding during only one or two pill cycles. Breakthrough bleeding without spotting occurred in 1% of all cycles, spotting without breakthrough bleeding in 9.3% of all cycles, and breakthrough bleeding with spotting in 3% of all cycles. Amenorrhea was obsd. in 3% of all cycles. In all, 20 subjects (6%) discontinued participation in the study because of

adverse events. No serious adverse events related to the study drug were reported. No clin. significant changes in wt., blood pressure, or lipids were reported. The impact of the new progestogen DRSP on the women's self-perception of menstrual health was also evaluated. Subjects reported that
symptoms of water retention, neg. affect, and increased appetite significantly improved at cycle 6 from baseline. This study demonstrates that Yasmin is an effective oral contraceptive that is safe and well tolerated.

SUPPL. TERM: Yasmin drospirenone progestogen oral contraceptive
INDEX TERM: Amenorrhea
Appetite
Blood pressure
Body weight
Hydration, physiological
Menstrual disorder
Ovarian cycle
(Yasmin low-dose combination oral contraceptive contg. drospirenone efficacy, safety and cycle control in
women)
INDEX TERM: Lipids, biological studies
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(blood; Yasmin low-dose combination oral contraceptive contg. drospirenone efficacy, safety and cycle control
in
women)
INDEX TERM: Contraceptives
(oral; Yasmin low-dose combination oral contraceptive contg. drospirenone efficacy, safety and cycle control
in
women)
INDEX TERM: 67392-87-4, Drospirenone
ROLE: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(Yasmin low-dose combination oral contraceptive contg. drospirenone efficacy, safety and cycle control in
women)
INDEX TERM: 164017-31-6, Ethinylestradiol-drospirenone mixt.
ROLE: ADV (Adverse effect, including toxicity); BAC (Biological
activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Yasmin; Yasmin low-dose combination oral contraceptive contg. drospirenone efficacy, safety and cycle control
in
women)
INDEX TERM: 57-88-5, Cholest-5-en-3-ol (3.beta.)-, biological studies
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(blood; Yasmin low-dose combination oral contraceptive contg. drospirenone efficacy, safety and cycle control
in
women)
REFERENCE COUNT: 17
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CAPLUS
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REFERENCE 4

ACCESSION NUMBER: 132:288794 CA
TITLE: Sympathetic nervous system activity-reducing agents for treatment of disease- or age-related weight loss and for enhancement of exercise performance
INVENTOR(S): Anker, Stefan Dietmar; Coats, Andrew Justin Stewart
PATENT ASSIGNEE(S): Imperial College Innovations Limited, UK
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-00
CLASSIFICATION: 1-12 (Pharmacology)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021509	A2	20000420	WO 1999-GB3302	19991015
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			GB 1998-22458	19981015
			GB 1998-22459	19981015
			GB 1999-17181	19990723

ABSTRACT:
A method of treating wt. loss due to underlying disease in a patient, the method comprising administering to the patient an effective amt. of an agent which reduces sympathetic nervous system activity. A method of treating wt. loss due to underlying disease in a patient, the method comprising administering to the patient an effective amt. of any one or more of the following: a compd. which inhibits the effect of aldosterone such as an aldosterone antagonist; a chymase inhibitor; a cathepsin B inhibitor; a .beta. receptor blocker; an imidazoline receptor antagonist; a centrally acting .alpha. receptor antagonist; a peripherally acting .alpha. receptor antagonist;
a ganglion blocking agent; a drug that has an effect on cardiovascular reflexes
and thereby reduces SNS activity such as an opiate; scopolamine; an endothelin receptor antagonist; and a xanthine oxidase inhibitor. The methods are particularly useful in treating cardiac cachexia. The sympathetic nervous system activity-reducing agents may also be used to treat wt. loss due to aging
and to enhance exercise performance.

SUPPL. TERM: sympathetic agent disease related wt loss; age related wt loss sympathetic agent; exercise performance cardiac cachexia sympathetic agent
INDEX TERM: Anabolic agents
(anabolic growth factors; sympathetic nervous system

tivity-reducing agents for treatment of disease- or e-related wt. loss and for enh ement of exercise performance)

INDEX TERM: Angiotensin receptor antagonists
(angiotensin II; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Endothelin receptors
Imidazoline receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Reflex
(cardiovascular; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Lung, disease
(chronic obstructive; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Infection
(chronic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Muscle
(elec. stimulation of; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Peptides, biological studies
ROLE: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epoxysuccinyl; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Heart, disease
Kidney, disease
(failure, chronic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Nervous system agents
(ganglionic blocking agents; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Body weight
(loss; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: AIDS (disease)
Aging, animal
Cachexia
Cirrhosis
Disease, animal
Emphysema
Exercise

Heart disease
Hypertension
Malnutrition
Neoplasm
Nervous system agents
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Opioids
ROLE: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Nervous system
(sympathetic; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Tumor necrosis factors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha., antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Adrenoceptor antagonists
(.alpha.-; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: Adrenoceptor antagonists
(.beta.-; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: 180384-56-9, Ro 61-1790
ROLE: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Ro 61-1790; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: 188307-16-6, T 0201
ROLE: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(T 0201; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: 52-39-1, Aldosterone
ROLE: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(and aldosterone antagonists; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: 9002-17-9, Xanthine oxidase 9004-08-4, Cathepsin 9015-82-1, Angiotensin-converting enzyme 9047-22-7, Cathepsin B 97501-92-3, Chymase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss

d for enhancement of exercise performance)

INDEX TERM: 90[redacted]72-6, Growth hormone 67763-9[redacted], IGF-1

ROLE: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study);

USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: 51-34-3, Scopolamine 52-01-7, Spironolactone 52-01-7D, Spironolactone, 15,16-methylene derivs. 57-27-2, Morphine, biological studies 60-26-4, Hexamethonium 60-30-0, Azamethonium 60-40-2, Mecamylamine 68-91-7 71-91-0, Tetraethylammonium bromide 100-33-4, Pentamidine 119-44-8, Xanthopterin 125-28-0, Dihydrocodeine 144-44-5, Pentolinium 315-30-0, Allopurinol 382-82-1 492-11-5, Leukopterin 497-23-4, 2(5H)-Furanone 525-66-6, Propranolol 546-48-5, Synapleg 555-30-6, .alpha.-Methyldopa 561-27-3, Diamorphine 968-93-4, Testolactone 971-60-8, Benzohexonium 1218-98-0, 7,8-Dihydroneopterin 2009-64-5, Neopterin 2365-25-5, Pentamethonium 2465-59-0, Oxypurinol 3613-69-2, Cypenam 3930-20-9, Sotalol 4138-96-9 4205-90-7, Clonidine 4844-10-4, Hexafluorenium 5472-41-3, 4-Amino-6-hydroxypyrazolo[3,4-d]pyrimidine 6452-71-7, Oxprenolol 7187-66-8, Trimetaphan 9087-70-1, Aprotinin 11096-26-7, Erythropoietin 13523-86-9, Pindolol 13655-52-2, Alprenolol 17528-72-2 19216-56-9, Prazosin 22150-76-1, Biopterin 22664-55-7, Metipranolol 26839-75-8, Timolol 29122-68-7, Atenolol 36894-69-6 37517-30-9, Acebutolol 38363-40-5, Penbutolol 42200-33-9, Nadolol 47141-42-4, Levobunolol 51384-51-1, Metoprolol 51781-06-7, Carteolol 52485-79-7, Buprenorphine 54187-04-1, Rilmenidine 56980-93-9, Celiprolol 63590-64-7, Terazosin 63659-18-7, Betaxolol 66376-36-1, Alendronate 66722-44-9 67392-87-4, Dihydrospirorenone 71119-11-4, Bucindolol 72956-09-3, Carvedilol 74191-85-8, Doxazosin 74220-07-8, Spirorenone 75438-57-2, Moxonidine 76676-33-0, RU26752 76684-89-4, E 64c 81147-92-4, Esmolol 86102-31-0, Tissue inhibitor of matrix metalloproteinase 87952-98-5, Mespirenone 91448-99-6, Cystatin C 93519-21-2 95847-70-4, Ipsapirone 107544-29-6, Stefin A 107724-20-9, Eplerenone 118457-14-0, Nebivolol 134448-10-5, CA-074 136553-74-7, WS 7338B 136553-81-6, BQ123 144602-02-8, IRL 1038 145380-08-1, RU40555 151039-33-7, PD 142893 156161-89-6, BQ-788 157659-79-5, SB 209670 162412-70-6, PD 156707 171714-84-4, LU135252 173189-01-0, IRL 3461 173937-91-2, ABT-627 193969-54-9, S-0139 204326-22-7, PD 164333 223756-43-2, A-216546 264276-89-3

ROLE: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: 75847-73-3, Enalapril 114798-26-4, Losartan

ROLE: BAC (Biological activity or effector, except adverse);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

INDEX TERM: 51-41-2, Noradrenaline 51-43-4, Epinephrine 11128-99-7, Angiotensin II 123626-67-5, Endothelin 1
ROLE: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(sympathetic nervous system activity-reducing agents for treatment of disease- or age-related wt. loss and for enhancement of exercise performance)

REFERENCE 5

ACCESSION NUMBER: 132:117958 CA
TITLE: Use of biogenic estrogen sulfamates for hormone replacement therapy
INVENTOR(S): Elger, Walter; Lahteenmaki, Pekka; Lehtinen, Matti; Reddersen, Gudrun; Zimmermann, Holger; Oettel, Michael; Schwarz, Sigfrid
PATENT ASSIGNEE(S): Jenapharm G.m.b.H & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K031-565
CLASSIFICATION: 2-4 (Mammalian Hormones)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006175	A1	20000210	WO 1999-DE1496	19990513
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19834931	A1	20000224	DE 1998-19834931	19980728
AU 9951481	A1	20000221	AU 1999-51481	19990513
PRIORITY APPLN. INFO.:			DE 1998-19834931	19980728
			WO 1999-DE1496	19990513

ABSTRACT:
The invention relates to the use of biogenic estrogen sulfamates for the oral discontinuous application for hormone replacement therapy (HRT). The discontinuous administration takes place in intervals ranging from 2 to 40 days. The invention also provides the addnl. application of gestagens, preferably continuously in the form of an implant or in the form of an intrauterine releasing system (IUD). Estrone sulfamate, estradiol sulfamate, or an N-acyl sulfamate of estrone, estradiol or estriol having up to 7 carbon atoms in the acyl chain, or a combination comprised of two or more of the active ingredients, are used as biogenic estrogen sulfamates.

SUPPL. TERM: biogenic estrogen sulfamate hormone replacement therapy
INDEX TERM: Hormone replacement therapy
(biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: Estrogens
Progestogens
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biogenic estrogen sulfamates for hormone replacement

erapy)
INDEX TERM: Dr[redacted] delivery systems
(implants; biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: Contraceptives
(intrauterine; biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: Drug delivery systems
(oral; biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: Menopause
(postmenopause; biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: Amides, biological studies
Sulfates, biological studies
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfamates; biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: 979-32-8, Estradiol valerate
ROLE: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: 50-27-1D, Estriol, N-acylsulfamate derivs. 50-28-2D, Estradiol, N-acylsulfamate derivs. 53-16-7D, Estrone, N-acylsulfamate derivs. 68-22-4, Norethisterone 71-58-9,
Medroxyprogesterone acetate 302-22-7, Chlormadinone acetate 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 3562-63-8, Megestrol 54024-22-5, Desogestrel 65928-58-7, Dienogest 67392-87-4, Drospirenone 148672-09-7 172377-52-5 175219-34-8
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biogenic estrogen sulfamates for hormone replacement therapy)
INDEX TERM: 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies 481-97-0, Estrone sulfate
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(biogenic estrogen sulfamates for hormone replacement therapy)
REFERENCE COUNT: 5
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(2) Elger, W; JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY 1995, V55(3-4), P395 MEDLINE
(3) Leiras Oy; WO 9501161 A 1995
(4) Michael, O; US 5633242 A 1997
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REFERENCE 6

ACCESSION NUMBER: 131:83108 CA
TITLE: Progesterone analogs similarly modulate endometrial matrix metalloproteinase-1 and matrix metalloproteinase-3 and their inhibitor in a model for
long-term contraceptive effects
AUTHOR(S): Hampton, A. L.; Nie, G.; Salamonsen, L. A.
CORPORATE SOURCE: Prince Henry's Institute of Medical Research, Clayton,
3168, Australia
SOURCE: Mol. Hum. Reprod. (1999), 5(4), 365-371
CODEN: MHREFD; ISSN: 1360-9947

PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 2-3 (Mammalian Hormones)
ABSTRACT:
Matrix metalloproteinases (MMPs) and their tissue inhibitors (TIMPs) are involved in normal menstruation while MMP-1 and MMP-3 prodn. by human endometrial stromal cells (HESCs) is repressed in vitro by progesterone. The authors postulated that the repression by synthetic progestins of MMP prodn. from HESCs may not be fully maintained in the long term, and that this may account for the disturbed uterine bleeding patterns in women using long-acting progestins. In this study, a long-term HESC culture model was established to compare the effects of natural progesterone and a no. of synthetic analogs (ORG2058 medroxyprogesterone acetate, norethindrone acetate, levonorgestrel and
drospirenone) on the prodn. by these cells of MMP-1 and MMP-3 and TIMP-1. Zymog. and enzyme-linked immunosorbent anal. of culture medium after 2 wk showed that both natural progesterone and all of the synthetic progestins tested maintained a significant inhibition of MMP-1 and MMP-3 prodn. Prodn. of
mRNA for MMP-1 and MMP-3 was also suppressed by all progestins, while TIMP prodn. was increased. Thus, menstrual bleeding disturbances which occur during
the use of synthetic progestins is not likely to result directly from changes in the effect of long-term progestin exposure on MMP-1 or MMP-3 or TIMP-1 prodn. by HESCs.

SUPPL. TERM: progesterone matrix metalloproteinase menstruation bleeding endometrium stroma contraceptive female
INDEX TERM: Menstrual disorder
(bleeding; progesterone analogs similarly modulate endometrial matrix metalloproteinase-1 and matrix metalloproteinase-3 and inhibitor TIMP in a model for long term contraceptive effects)
INDEX TERM: Uterus
(endometrium, stroma; progesterone analogs similarly modulate endometrial matrix metalloproteinase-1 and matrix metalloproteinase-3 and inhibitor TIMP in a model for long term contraceptive effects)
INDEX TERM: Contraceptives
(female; progesterone analogs similarly modulate endometrial matrix metalloproteinase-1 and matrix metalloproteinase-3 and inhibitor TIMP in a model for long term contraceptive effects)
INDEX TERM: Progestogens
ROLE: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(progesterone analogs similarly modulate endometrial matrix metalloproteinase-1 and matrix metalloproteinase-3
and inhibitor TIMP in a model for long term contraceptive
effects)
INDEX TERM: 51-98-9, Norethindrone acetate 57-83-0, Progesterone, biological studies 71-58-9, Medroxyprogesterone acetate 797-63-7, Levonorgestrel 24320-06-7, Org2058 67392-87-4,
Drospirenone
ROLE: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(progesterone analogs similarly modulate endometrial matrix metalloproteinase-1 and matrix metalloproteinase-3
and inhibitor TIMP in a model for long term contraceptive

[redacted]fects)
INDEX TERM: 90[redacted]12-1, MMP-1 79955-99-0, MMP-[redacted] 140208-24-8, TIMP-1
ROLE: BPR (Biological process); MFM (Metabolic formation); BIOL
(Biological study); FORM (Formation, nonpreparative); PROC (Process)
(progesterone analogs similarly modulate endometrial matrix metalloproteinase-1 and matrix metalloproteinase-3
and inhibitor TIMP in a model for long term contraceptive
effects)

REFERENCE COUNT: 27
(1) Bruner, K; Proc Natl Acad Sci USA 1995, V92, P7362 CAPLUS
(2) Clark, D; Hum Reprod 1996, V11, P1438 MEDLINE
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(5) Hampton, A; Biol Reprod 1995, V53, P302 CAPLUS
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CAPLUS
(16) Riedy, M; BioTechniques 1995, V18, P70 CAPLUS
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CAPLUS
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(27) Zhang, J; Biol Reprod 1999, V59, P693

REFERENCE 7

ACCESSION NUMBER: 130:347882 CA
TITLE: Oral contraceptives containing antiestrogen and progestin
INVENTOR(S): Gast, Michael Jay; Miller, Christopher Paul
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-00
CLASSIFICATION: 2-3 (Mammalian Hormones)
Section cross-reference(s): 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9924027	A2	19990520	WO 1998-US23427	19981104
WO 9924027	A3	19990715		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9913031	A1	19990531	AU 1999-13031	19981104
BR 9813982	A	20000926	BR 1998-13982	19981104
EP 1051179	A2	20001115	EP 1998-956525	19981104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
NO 2000002167	A	20000628	NO 2000-2167	20000427
PRIORITY APPLN. INFO.:			US 1997-965083	19971106
			US 1997-66089	19971117
			US 1997-66090	19971117
			US 1997-66095	19971117
			US 1997-66100	19971117
			WO 1998-US23427	19981104

ABSTRACT:
This invention provides a method of providing contraception which comprises administering to a female of child-bearing age a combination of a non-uterotrophic anti-estrogen and a progestin for 28 days/28-day menstrual cycle. When 2-(4-hydroxyphenyl)-3-methyl-1-[4-(2-(azepan-1-yl)ethoxy)benzyl]-1H-indol-5-ol (I) and levonorgestrel are administered according to a 28-day monophasic regimen, the dosage with I at 2 mg and levonorgestrel at 90 .mu.g is
preferred.

SUPPL. TERM: contraceptive oral antiestrogen progestin
INDEX TERM: Oral contraceptives
Ovarian cycle
(oral contraceptives contg. antiestrogen and progestin)
INDEX TERM: Antiestrogens
Progestins
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral contraceptives contg. antiestrogen and progestin)
INDEX TERM: 51-98-9, Norethisterone acetate 68-22-4, Norethindrone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 1845-11-0, Nafoxidine 6533-00-2, Norgestrel 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-KetoDesogestrel 60282-87-3, Gestodene 65928-58-7, Dienogest 67392-87-4, Drospirenone 74513-62-5, Trimegestone 78994-23-7, Levormeloxifene 82413-20-5, Droloxifene 84449-90-1, Raloxifene 89778-26-7, Toremifene 105149-04-0, Osaterone 115767-74-3, TAT-59 116057-75-1, Idoxifene 129453-61-8, ICI-182780
165536-41
-4, MDL-103323 182133-25-1, Benzo[b]thiophene-6-ol, 2-(4-methoxyphenyl)-3-[4-[2-(1-piperidinyl)ethoxy]phenoxy]-182133-27-3 182167-03-9, EM-800 190791-29-8, CP-336156

198[redacted]-18-1 198480-19-2 198480-[redacted]-5 198480-21-6
198[redacted]-30-7 198480-31-8 198480-[redacted] 198480-33-0
198480-34-1 198480-35-2 198480-36-3 198480-37-4
198480-38-5 198480-39-6 198480-41-0 198480-42-1
198480-43-2 198480-44-3 198480-45-4 198480-46-5
198480-47-6 198480-48-7 198480-49-8 198480-50-1
198480-51-2 198480-52-3 198480-53-4 198480-54-5
198480-55-6 198480-56-7 198480-74-9 198480-75-0
198480-76-1 198480-77-2 198480-78-3 198480-79-4
198480-80-7 198480-83-0 198480-84-1 198480-85-2
198480-86-3 198480-87-4 198480-88-5 198480-89-6
198480-90-9 198480-91-0 198480-92-1 198480-93-2
198480-94-3 198480-95-4 198480-96-5 198480-97-6
198481-17-3 198481-18-4 198481-32-2 198481-38-8
198481-39-9 224801-40-5
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral contraceptives contg. antiestrogen and progestin)

REFERENCE 8

ACCESSION NUMBER: 130:242332 CA
TITLE: Oral contraceptive preparation having a first phase comprising progestin/estrogen and a second phase comprising progestin
INVENTOR(S): Gast, Michael Jay
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-56
CLASSIFICATION: 63-6 (Pharmaceuticals)
Section cross-reference(s): 2
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9913882	A1	19990325	WO 1998-US18850	19980909
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9892286	A1	19990405	AU 1998-92286	19980909
EP 1011681	A1	20000628	EP 1998-944837	19980909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			US 1997-928530	19970912
			WO 1998-US18850	19980909

ABSTRACT:
A method of contraception comprises administering to a female of child-bearing age for 28 days per menstrual cycle a combination of a progestin at a daily dosage equiv. to 30-150 .mu.g levonorgestrel and an estrogen at a daily dosage equiv. to 10-20 .mu.g ethynylestradiol for 23-25 days beginning on day 1 of the
menstrual cycle, followed by administering a progestin at a daily dosage equiv.
to 10-100 .mu.g levonorgestrel for 3-5 days. This regimen provides effective contraception, good cycle control, and minimal side effects while greatly

reducing the total co[redacted]ceptive steroid administered p[redacted] 28-day cycle. A suitable regimen comp[redacted]ed administration of levonorge[redacted]el 75 and ethynylestradiol 15 .mu.g/day for the first 24 cycle days, followed by levonorgestrel 37.5 .mu.g/day for the last 4 days.

SUPPL. TERM: oral contraceptive progestin estrogen; levonorgestrel ethynylestradiol oral contraceptive
INDEX TERM: Oral contraceptives
(oral contraceptive prepn. with first phase comprising progestin/estrogen and second phase comprising progestin)
INDEX TERM: Conjugated estrogens
Estrogens
Progestins
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral contraceptive prepn. with first phase comprising progestin/estrogen and second phase comprising progestin)
INDEX TERM: 50-28-2, 17.beta.-Estradiol, biological studies 51-98-9, Norethisterone acetate 53-16-7, Estrone, biological studies 57-63-6, Ethynylestradiol 68-22-4, Norethindrone
72-33-3, Mestranol 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 6533-00-2, Norgestrel 35189-28-7, Norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 60282-87-3, Gestodene 65928-58-7, Dienogest 67392-87-4, Drospirenone 74513-62-5, Trimegestone 105149-04-0, Osaterone
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral contraceptive prepn. with first phase comprising progestin/estrogen and second phase comprising progestin)
REFERENCE COUNT: 1
(1) Akzo, N; EP 0368373 A 1990

REFERENCE 9

ACCESSION NUMBER: 130:100684 CA
TITLE: Oral contraceptive comprising progestin/estrogen combination
INVENTOR(S): Gast, Michael J.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K009-20
SECONDARY: A61K031-56
US PATENT CLASSIF.: 424464000
CLASSIFICATION: 63-6 (Pharmaceuticals)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5858405	A	19990112	US 1997-887162	19970702

ABSTRACT:
A bridged triphasic combination progestin/estrogen oral contraceptive regimen is provided comprising the administration of a contraceptive progestin/estrogen combination for 23-25 days consecutive days beginning on the first day of menses, followed by the administration of an estrogen for 3-5 days following

the administration of the estrogen/progestin combination so that the total period of administration is 28 days per 28 day cycle. Particularly preferred progestins of this invention are trimegestone, dienogest, and drospirenone. A tablet contained trimegestone 125, ethinyl estradiol 15, microcryst. cellulose,
lactose, polaciillin potassium, magnesium stearate, Opadry pink, polyethylene glycol, and water q.s. for a tablet.

SUPPL. TERM: oral contraceptive tablet progestin estrogen; trimegestone ethinyl estradiol oral contraceptive tablet
INDEX TERM: Oral contraceptives
(oral contraceptive comprising progestin/estrogen combination)
INDEX TERM: Conjugated estrogens
Estrogens
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral contraceptive comprising progestin/estrogen combination)
INDEX TERM: 50-28-2, .beta. Estradiol, biological studies 57-63-6, Ethinyl estradiol 57-83-0, Progestin, biological studies 72-33-3, Mestranol 65928-58-7, Dienogest 67392-87-4, Drospirenone. 74513-62-5, Trimegestone
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral contraceptive comprising progestin/estrogen combination)
REFERENCE COUNT: 23

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(2) Anon; DE 4104385 1992 CAPLUS
(3) Anon; EP 0628312 1994
(4) Anon; DE 4313926 1994 CAPLUS
(5) Anon; WO 9517194 1995
(6) Anon; WO 9526730 1995
(7) Anon; EP 0696454 1996
(8) Bennink; US 5418228 1995
(9) Bergink; US 5262408 1993
(10) Boissonneault; US 4962098 1990 CAPLUS
(11) Coussediere; US 4273771 1981
(12) Edgren; US 4390531 1983
(13) Ehrlich; US 5280023 1994
(14) Gast; US 5747480 1998 CAPLUS
(15) Lachnit-Fixson; US 3957982 1976
(16) Lachnit-Fixson; US 3969502 1976 CAPLUS
(17) Lachnit-Fixson; US 4621079 1986
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(23) Spona; US 5583129 1996

REFERENCE 10

ACCESSION NUMBER: 129:77031 CA
TITLE: Therapeutic gestagens for premenstrual dysphoric disorder
INVENTOR(S): Nashed, Norman
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.:
MAIN: A61K031-57

SECONDARY: A61K031-565
CLASSIFICATION: 2-4 (Mammalian Hormones)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19654609	A1	19980625	DE 1996-19654609	19961220
WO 9827929	A2	19980702	WO 1997-DE3032	19971222
WO 9827929	A3	19981105		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9859810	A1	19980717	AU 1998-59810	19971222
PRIORITY APPLN. INFO.:			DE 1996-19654609	19961220
			WO 1997-DE3032	19971222

ABSTRACT:
Gestagens such as drospirenone, cyproterone acetate, and dienogest (optionally in combination with natural or synthetic estrogens such as estradiol or ethynylestradiol) are useful in prepn. of medications for treatment of premenstrual dysphoric disorder, possibly owing to their antiandrogenic action.
Thus, women with premenstrual dysphoric disorder, treated daily with 3 mg drospirenone and 30 .mu.g ethynylestradiol orally on days 1-21 of the menstrual
cycle for 4-6 cycles, showed a lessening of symptoms related to mood, appetite,
sleep, etc.

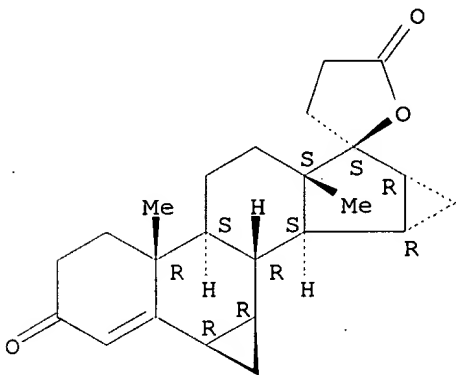
SUPPL. TERM: premenstrual dysphoria treatment gestagen
INDEX TERM: Premenstrual syndrome
(therapeutic gestagens for premenstrual dysphoric disorder)
INDEX TERM: Estrogens
Progestins
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic gestagens for premenstrual dysphoric disorder)
INDEX TERM: 50-28-2, Estradiol, biological studies 50-28-2D, Estradiol, esters 57-63-6, Ethynylestradiol 427-51-0, Cyproterone acetate 979-32-8, Estradiol valerate 65928-58-7, Dienogest 67392-87-4, Drospirenone
ROLE: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic gestagens for premenstrual dysphoric disorder)

L2 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2000 ACS
RN 67372-75-2 REGISTRY
CN Spiro[17H-dicyclopropa[6,7:15,16]cyclopenta[a]phenanthrene-17,2'(5'H)-furan]-3,5'(2H)-dione, 1,3',4',6,7,8,9,10,11,12,13,14,15,16,20,21-hexadecahydro-10,13-dimethyl-,
[6R-(6.alpha.,7.alpha.,8.beta.,9.alpha.,10.beta.,13.beta.,14.alpha.,15.beta.,16.beta.,17.beta.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H30 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL
(*File contains numerically searchable property data)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C3-C3-C4O-C5-C6-C6-C6	C3-C3-OC4-C5-C6-C6-C6	3-3-5-5-6-6-6	C22O	21803.1.1	1

Absolute stereochemistry.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1

ACCESSION NUMBER: 95:25402 CA
TITLE: 6.beta.,7.beta.; 15,16-Dimethylene-1,4-androstadien-3-ones
INVENTOR(S): Wiechert, Rudolf; Bittler, Dieter; Kerb, Ulrich; Prezewowsky, Klaus; Casals-Stenzel, Jorge; Losert, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.: C07J053-00; C07J021-00; A61K031-565
CLASSIFICATION: 32-5 (Steroids)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2922500	A1	19801204	DE 1979-2922500	19790531
EP 19690	A1	19801210	EP 1980-101383	19800317
EP 19690	B1	19820421		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AT 880	E	19820515	AT 1980-101383	19800317
SU 873890	A3	19811015	SU 1980-2907605	19800411
AU 8058745	A1	19801204	AU 1980-58745	19800526
AU 531057	B2	19830811		
JP 55162799	A2	19801218	JP 1980-69079	19800526
JP 02014360	B4	19900406		

CS 214712	[redacted]	19820528	CS 1980-371[redacted]	19800527
ES 491916	[redacted]	19801216	ES 1980-491[redacted]	19800528
US 4291029	A	19810922	US 1980-154194	19800529
DD 151172	C	19811008	DD 1980-221451	19800529
IL 60185	A1	19830615	IL 1980-60185	19800529
DK 8002347	A	19801201	DK 1980-2347	19800530
DK 145140	B	19820913		
DK 145140	C	19830221		
CA 1134814	A1	19821102	CA 1980-353151	19800530
HU 24323	O	19830128	HU 1980-1372	19800530
HU 181714	B	19831128		
HU 30744	O	19840328	HU 1982-3323	19800530
HU 187419	B	19860128		

PRIORITY APPLN. INFO.: DE 1979-2922500 19790531
EP 1980-101383 19800317

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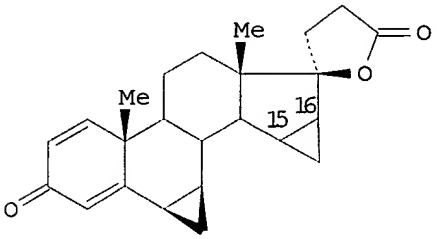

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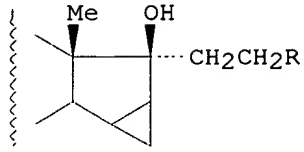
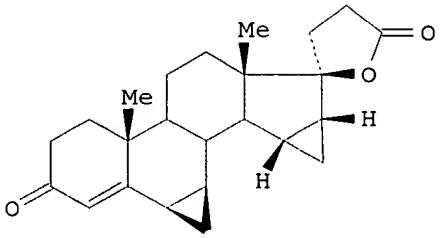


II



III

ABSTRACT:
Dimethyleneandrostadienes I and II (R = CH2OH, CO2K) were prepd. and they possessed diuretic activity (no data). Thus, treatment of androstene lactone III with SeO2 in Me3COH contg. HOAc gave 15.alpha.,16.alpha.-I. Dichlorodicyanobenzoquinone was also used as a dehydrogenation reagent.

SUPPL. TERM: dimethyleneandrostadienone prepn diuretic; dehydrogenation dimethyleneandrostenone; androstadienone dimethylene prepn diuretic

INDEX TERM: Diuretics
(dimethyleneandrostadienone spiro lactones)

INDEX TERM: Dehydrogenation
(of dimethyleneandrostenones)

INDEX TERM: Steroids, preparation
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, of dimethyleneandrostadienones)

INDEX TERM: 67372-75-2 67392-87-4 69651-50-9
ROLE: RCT (Reactant)
(dehydrogenation of)

INDEX TERM: 74220-07-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)

INDEX TERM: 77579-18-1P 77593-18-1P 77646-30-1P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

REFERENCE 2

ACCESSION NUMBER: 89:110129 CA
TITLE: Spirolactones
INVENTOR(S): Wiechert, Rudolf; Bittler, Dieter; Kerb, Ulrich; Vasals-Stenzel, Jorge; Losert, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Ger.
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
INT. PATENT CLASSIF.: C07J019-00
CLASSIFICATION: 32-6 (Steroids)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2652761	A1	19780518	DE 1976-2652761	19761116
DE 2652761	C2	19851121		
NL 7711946	A	19780518	NL 1977-11946	19771031
SU 695560	D	19791030	SU 1977-2537651	19771103
CH 631463	A	19820813	CH 1977-13616	19771108
AU 7730509	A1	19790517	AU 1977-30509	19771109
AU 512611	B2	19801016		
IL 53353	A1	19820430	IL 1977-53353	19771110
US 4129564	A	19781212	US 1977-850524	19771111
DD 132968	C	19781122	DD 1977-202077	19771114
DD 132968	B3	19910328		
SE 7712891	A	19780517	SE 1977-12891	19771115
SE 436425	B	19841210		
SE 436425	C	19850321		
GB 1550568	A	19790815	GB 1977-47440	19771115
AT 7708155	A	19791015	AT 1977-8155	19771115
AT 356827	B	19800527		
HU 174983	P	19800428	HU 1977-SC630	19771115
BE 860877	A1	19780516	BE 1977-182661	19771116
DK 7705080	A	19780517	DK 1977-5080	19771116
DK 141967	B	19800728		
DK 141967	C	19801208		
JP 53063373	A2	19780606	JP 1977-137758	19771116
JP 61056240	B4	19861201		
FR 2370755	A1	19780609	FR 1977-34434	19771116
FR 2370755	B1	19800606		
ES 464193	A1	19780901	ES 1977-464193	19771116
CS 194823	P	19791231	CS 1977-7551	19771116
CA 1092094	A1	19801223	CA 1977-291065	19771116
DK 7804542	A	19781012	DK 1978-4542	19781012
DK 142951	B	19810302		
DK 142951	C	19810907		
SU 743582	D	19800625	SU 1979-2706061	19790111
AT 7904289	A	19810815	AT 1979-4289	19790618
AT 366391	B	19820413		
CH 632774	A	19821029	CH 1982-793	19820209
JP 61218595	A2	19860929	JP 1985-212779	19850927
JP 02042840	B4	19900926		

PRIORITY APPLN. INFO.:

DE 1976-2652761	19761116
CH 1977-13616	19771108
AT 1977-8155	19771115
DK 1977-5080	19771116

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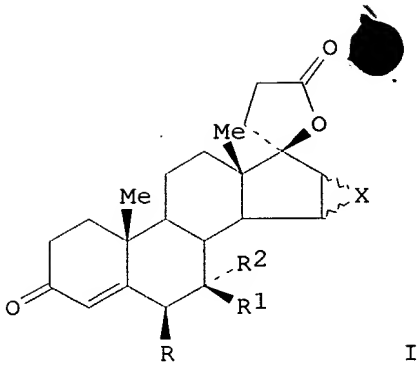

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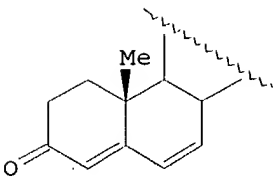

II

ABSTRACT:
Diuretic (no data) spiroandrostenefuranones I [RR1 = CH2, R2 = H; R = R1 = H, R2 = R3COS (R3 = C1-5 alkyl); X = 15.alpha.,16.alpha.-CH2, 15.beta.,16.beta.-CH2, bond] (9 compds.)) were prepd. a) by treatment of II with R3COSH in a protic solvent and b.) methylenation of II by Me3S+(O) I--NaH in aprotic solvent. Thus, 1.5 g II (X = bond) and 1.5 mL AcSH in MeOH refluxed 2 h gave 1.05 g I (X = bond, R = R1 = H, R2 = AcS). To a soln. of 4.13 g Me3S+(O) I- in
Me2SO contg. 512 mg 80% NaH was added 3.09 g II (X = bond) and the mixt. refluxed 24 h to give 520 mg I (X = bond, RR1 = CH2, R2 = H).

SUPPL. TERM: methylenation spiroandrostenefuranone; androstene spirofuran; furanone spiroandrostene; methylenespiroandrostenefuran prepn diuretic; thioacylation spiroandrostenefuran

INDEX TERM: Methylenation
(of spiroandrostadienefuranones)

INDEX TERM: Diuretics
(spiroandrostenefuranones)

INDEX TERM: Steroids, preparation
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(spiro[17,2'-furan], 3,5'-dioxo-4-unsatd., prepn. of)

INDEX TERM: 67372-56-9P 67372-63-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and bromination of)

INDEX TERM: 67372-59-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of)

INDEX TERM: 55534-25-3P 67372-57-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dehydrobromination of)

INDEX TERM: 67372-68-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dehydrogenation of)

INDEX TERM: 67372-55-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and enolization-alkylation of)

INDEX TERM: 67372-62-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and enolization-ethylation of)

INDEX TERM: 67372-52-5P 67372-66-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis-cyclization of)

INDEX TERM: 673[illegible]54-7P
ROLE: [illegible] (Reactant); SPN (Synthetic p[illegible]aration); PREP (Preparation)
(prepn. and hydrolysis-oxidn. of)

INDEX TERM: 67372-53-6P 67372-60-5P 67372-61-6P 67372-67-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn. of)

INDEX TERM: 67372-58-1P 67372-64-9P 67372-69-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reactions of)

INDEX TERM: 67372-70-7P 67372-71-8P 67372-72-9P 67372-73-0P
67372-74-1P 67372-75-2P 67372-76-3P 67392-86-3P
67392-87-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

INDEX TERM: 17921-63-0 38002-07-2 67372-65-0
ROLE: RCT (Reactant)
(reaction of, with bromodimethoxypropane)

INDEX TERM: 36255-44-4
ROLE: RCT (Reactant)
(reaction of, with hydroxyandrostadienone)

INDEX TERM: 507-09-5, reactions 1892-31-5
ROLE: RCT (Reactant)
(reaction of, with spiroandrostadienefurans)